

Commentary on Lande-Arnold Analysis

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Abstract

A solution to the problem of estimating fitness landscapes was proposed by Lande and Arnold (1983). Another solution, which avoids problematic aspects of the Lande-Arnold methodology, was proposed by Shaw, Geyer, Wagenius, Hangelbroek, and Etterson (2008). This technical report goes through Lande-Arnold theory in detail paying careful attention to problematic aspects. The only completely new material is a theoretical analysis of when the best quadratic approximation to a fitness landscape, which is what the Lande-Arnold method estimates, is a good approximation to the actual fitness landscape.

1 Introduction

1.1 Fitness Landscapes

By “fitness landscape” we mean the conditional expectation of fitness w given a vector of phenotypic character variables z , considered as a function of those variables

$$g(z) = E(w \mid z). \quad (1)$$

Arnold (2003) discusses this concept, calling it the “adaptive landscape for phenotypic traits” and attributing it to Simpson (1944) who modified the original “adaptive landscape” concept of Wright (1932), which was the conditional expectation of w given a vector of genotypes. What we are calling the “fitness landscape” has also been called the “individual selection surface” by Phillips and Arnold (1989).

Statisticians call a conditional expectation like (1) considered as a function of the conditioning variable a *regression function* (Lindgren, 1993, p. 95) to emphasize that the primary objective of a regression program is to estimate the regression function (the conditional expectation of the response variable given the predictor variables). This is clear in non-parametric regression (Hastie and Tibshirani, 1990; Bowman and Azzalini, 1997) where the direct objective is to estimate the regression function, whatever it may be. It is less clear in parametric regression, whether ordinary least squares (OLS), generalized linear model (GLM), or something else, because the attention of users is often focused on regression coefficients rather than on predicted values and how well the predicted values estimate the true unknown regression function. Nevertheless, especially when parametric and nonparametric approaches are being compared, the only criterion by which they can be compared is how well they estimate the regression function.

Geyer, Wagenius and Shaw (2007) introduced a new class of statistical models, called *aster models*, designed specifically for modeling fitness. They are a generalization of GLM that can be used to estimate fitness landscapes, if fitness satisfies the assumptions for them, which it may do. Shaw, Geyer, Wagenius, Hangelbroek, and Etterson (2008) give examples of several kinds of life history analysis using aster models, including two in which fitness landscapes are estimated.

Napoleon famously said “If you want to take Vienna, take Vienna.” Our main advice in this paper is just as direct: if you want to estimate the fitness landscape, estimate the fitness landscape. Aster models enable us to do just that.

1.2 Lande-Arnold Analysis

Lande and Arnold (1983) offered a methodology that uses OLS regression to estimate quantities related to the fitness landscape, and it has since been very widely used. It makes only very weak assumptions about the distribution of w , but makes the strong assumption that z is multivariate normal.

1.2.1 Parameters

First, define

$$Q(\alpha, \beta, \gamma) = E\{(w - \alpha - z^T \beta - \frac{1}{2} z^T \gamma z)^2\}, \quad (2)$$

where α is a scalar, β a vector, and γ a symmetric matrix. Let α_1 and β_1 be the values that minimize $Q(\alpha, \beta, 0)$, which we assume to be unique, and let α_2 , β_2 , and γ_2 be the values that minimize $Q(\alpha, \beta, \gamma)$, which we also assume to be unique. Then

$$g_1(z) = \alpha_1 + z^T \beta_1 \quad (3a)$$

$$g_2(z) = \alpha_2 + z^T \beta_2 + \frac{1}{2} z^T \gamma_2 z \quad (3b)$$

are the *best linear approximation* and the *best quadratic approximation* (Phillips and Arnold, 1989) to the fitness landscape $g(z)$, where “best” means minimizing (2).

Second, define

$$\beta_3 = E\{\nabla g(z)\} \quad (4a)$$

$$\gamma_3 = E\{\nabla^2 g(z)\} \quad (4b)$$

where $\nabla g(z)$ denotes the vector of partial derivatives $\partial g(z)/\partial z_i$ and $\nabla^2 g(z)$ denotes the matrix of second partial derivatives $\partial^2 g(z)/\partial z_i \partial z_j$.

Third, define

$$\beta_4 = \Sigma^{-1} \text{cov}(w, z) \quad (5a)$$

$$\gamma_4 = \Sigma^{-1} \text{cov}(w, z z^T) \Sigma^{-1} \quad (5b)$$

where $\Sigma = \text{var}(z)$. Each of these betas is a vector, and each of these gammas is a symmetric matrix, in both cases the dimension being the same as for z .

We have $\beta_1 = \beta_4$ whenever these quantities are well defined. Under the assumption that z is multivariate normal with non-singular variance matrix α_1 , β_1 , α_2 , β_2 , and γ_2 are uniquely defined and $\beta_1 = \beta_3 = \beta_4$ and $\gamma_2 = \gamma_3 = \gamma_4$. Under the same assumption plus the additional assumption that $E(z) = 0$, we have $\beta_1 = \beta_2 = \beta_3 = \beta_4$. All of these identities were shown by Lande and Arnold (1983).

Lande and Arnold (1983) do not distinguish between these different betas and gammas, because they work under the assumptions just given that make them all equal. They call any of the betas the *directional selection gradient*. They call any of the gammas the *stabilizing or disruptive selection gradient*. It is important to understand, however, that if z is not multivariate normal, then all of these betas and gammas can be different (except $\beta_1 = \beta_4$ holds without normality) and it is necessary to be clear about which are being discussed.

The pairs β_2 and γ_2 and β_3 and γ_3 have relationships to the fitness landscape that are inherent in their definitions. The pair β_4 and γ_4 is loosely related to selection. In selection

not involving differential reproduction, the term $\text{cov}(w, z)$ is the change in the mean of z before and after selection. Conversely if we suppose a quantitative genetic model with additive genetic effect x that is conditionally independent of w given z , then β_4 is part of the change of mean of x before and after selection. There are similar, though looser, connections between γ_4 and the change of variance before and after selection. Details are given in Section 2.4. Lande and Arnold (1983) argue that the betas and gammas are more direct indicators of selection than any of these changes in means and variances due to selection. For example, a component of z not under direct selection will nevertheless be correlated with w if it is correlated with other components of z that are directly selected. The betas and gammas, being more directly related to the fitness landscape, more directly measure the effect of fitness on phenotype.

1.2.2 Estimators

Lande and Arnold (1983) propose using OLS regression to estimate these quantities. Define

$$Q_n(\alpha, \beta, \gamma) = \sum_{i=1}^n (w_i - \alpha - z_i^T \beta - \frac{1}{2} z_i^T \gamma z_i)^2, \quad (6)$$

where (w_i, z_i) are observed fitness and phenotype vectors for n individuals, let $\hat{\alpha}_1$ and $\hat{\beta}_1$ denote the minimizers of $Q_n(\alpha, \beta, 0)$, and let $\hat{\alpha}_2$, $\hat{\beta}_2$, and $\hat{\gamma}_2$ denote the minimizers of (6). We call attention to the obvious estimators $\hat{\beta}_4$ and $\hat{\gamma}_4$ obtained by plugging empirical variances and covariances into (5a) and (5b) in place of theoretical variances and covariances. One always has $\hat{\beta}_1 = \hat{\beta}_4$, an algebraic identity, but generally $\hat{\beta}_1 \neq \hat{\beta}_2$ and $\hat{\gamma}_2 \neq \hat{\gamma}_4$, even if the distribution of z is multivariate normal and $E(z) = 0$. Lande and Arnold (1983) note that $\hat{\beta}_1 \neq \hat{\beta}_2$ and propose using orthogonal polynomials to force equality here. However, even if $\beta_1 = \beta_2$, estimators are never equal to the parameters they estimate, so there is no reason to force equality between $\hat{\beta}_1$ and $\hat{\beta}_2$. When one considers that in real data z is never exactly multivariate normal, so $\beta_1 \neq \beta_2$, it is clearly inadvisable to change the definitions of $\hat{\beta}_2$ and $\hat{\gamma}_2$ so that they are no longer natural estimators of β_2 and γ_2 .

If our inference is conditional on z , then by the Gauss-Markov theorem Lindgren (1993, p. 510) $\hat{\alpha}_1$, $\hat{\beta}_1$, $\hat{\alpha}_2$, $\hat{\beta}_2$, and $\hat{\gamma}_2$ are best linear unbiased estimators (BLUE) of their corresponding parameters, where BLUE means they have the smallest variance of all linear unbiased estimators. Moreover, if we define the corresponding estimates of the best linear and quadratic approximations, which are the functions

$$\hat{g}_1(z) = \hat{\alpha}_1 + z^T \hat{\beta}_1 \quad (7)$$

$$\hat{g}_2(z) = \hat{\alpha}_2 + z^T \hat{\beta}_2 + \frac{1}{2} z^T \hat{\gamma}_2 z \quad (8)$$

then $\hat{g}_i(z)$ is the BLUE of $g_i(z)$ where BLUE means they have the smallest variance of all linear unbiased estimators (for $i = 1$ and $i = 2$ and for all z).

These estimators, however, have no other desirable properties. When nothing is assumed about the conditional distribution of w given z (and Lande and Arnold, 1983, make no such assumptions) nothing can be said about the sampling distributions of the estimators $\hat{\beta}_1$, $\hat{\beta}_2$, and $\hat{\gamma}_2$, and no confidence intervals or hypothesis tests for them can be derived. In particular, the confidence intervals and hypothesis tests that are printed out by OLS software have no validity.

This is well understood (see Mitchell-Olds and Shaw, 1987; Stanton and Thiede, 2005, and references cited therein). Any attempt to transform w to make it more normal, for example, doing OLS regression of $\log(1+w)$ on z is biologically wrong (Stanton and Thiede, 2005). To estimate the fitness landscape, one must regress w (untransformed) on z because the fitness landscape is the conditional expectation of w (untransformed) given z . Moreover, the distribution of w often has a large atom at zero resulting from individuals that die before reproducing, and no transformation can make that atom go away. Hence no transformation of w can be even approximately normal.

If z fails to be multivariate normal, then the OLS estimators have no known relationship to (4a), (4b), and (5b). One might hope for approximate equalities $\beta_1 \approx \beta_2 \approx \beta_3 \approx \beta_4$ and $\gamma_2 \approx \gamma_3 \approx \gamma_4$ if z is only approximately multivariate normal, but the argument of Lande and Arnold (1983) involves first and second partial derivatives of the probability density function of the multivariate normal distribution and the fact that third central moments of that distribution are zero and that fourth central moments have a relationship to the variance matrix given by the unnumbered displayed equation in Lande and Arnold (1983) following their equation (17). Thus one could only expect these approximate equalities if the first and second partial derivatives of the probability density function and the third and fourth central moments of z agree closely with those of a multivariate normal distribution having mean zero and variance matrix equal to that of z . This is a very strong requirement. Since statistical methodology for transformation to multivariate normality is rather crude (Andrews, Gnanadesikan, and Warner, 1971; Riani, 2004), there is no way these assumptions can be achieved in practice.

1.2.3 A Digression about the Applicability of Least Squares

Lande and Arnold (1983, pp. 1212–1213) include a curious defense of their use of OLS regression

In view of [their equation] (4), the vector $\beta = P^{-1}s$ [our equation (5a), hence our β_4] is a set of partial regression coefficients of relative fitness on the characters (Kendall and Stuart, 1973, eq. 27.42). Under quite general conditions, the method of least squares indicates that the element β_i gives the slope of the straight line that best describes the dependence of relative fitness on character z_i , after removing the residual effects of other characters on fitness (Kendall and Stuart, 1973, Ch. 27.15). There is no need to assume that the actual regressions of fitness on the characters are linear, or that the characters have a multivariate normal distribution. For this reason, the partial regression coefficients β provide a general solution to the problem of measuring the forces of directional selection acting directly on the characters.

To anyone who has taken a modern course in regression, from, say, Weisberg (2005), the notion that there is no need to assume actual regression function has the form incorporated in the model (“no need to assume ... that the actual regressions ... are linear”) seems to completely misunderstand linear regression. However, the cited reference (Kendall and Stuart, 1973, Ch. 27.15) does seem to say something of the sort

In our discussion from [Section] 27.8 onwards we have taken the regression relationship to be exactly linear, of type (27.18). Just as in [Section] 26.8,

we now consider the question of fitting regression relationships of this type to observed populations, whose regressions are almost never exactly linear, and by the same reasoning as there, we are led to the Method of Least Squares. [Some mathematical details of OLS regression follow.] ... (27.44) is identical with (27.19). Thus, as in [Section] 26.8, we reach the conclusion that the Least Squares approximation gives us the same regression coefficients as in the case of exact linearity of regression.

It follows that all of the results of this chapter are valid when we fit regressions by Least Squares to observed populations.

Thus Kendall and Stuart (1973) do seem to also argue that it is not necessary to assume “the regression relationship [is] exactly linear” but what is their argument? Actually, they have two. The argument of their Section 26.8, which is referred to in their Section 27.15 cited by Lande and Arnold and quoted above, culminates in

We have thus reached the conclusion that the calculation of an approximate regression line by the Method of Least Squares gives results which are the same as the correct ones in the case of exact linearity of regression.

which is echoed in their Section 27.15. This essentially says that when the regression function is exactly linear, that is, specialized to fitness landscapes, when $g = g_1$, then OLS does the right thing, but this is not in dispute. What about when the fitness landscape is not linear, when $g \neq g_1$, what does this argument say about that case? Nothing!

The second argument of Section 27.15 of Kendall and Stuart (1973) is in the part “... (27.44) is identical with (27.19)” in our quotation above that makes no sense without reference to a large amount of the notation of Kendall and Stuart, which we do not wish to repeat. The gist of this argument is that when the regression function is linear it is given by their equation (27.18), which in our notation is

$$g(z) = E(w \mid z) = \alpha + \beta_1 z_1 + \cdots \beta_k z_k \tag{9}$$

(except that Kendall and Stuart are assuming $\alpha = 0$ at this point), and the terminology Kendall and Stuart use for the β_i is *partial regression coefficients*, introduced just before the cited equation (27.18). In the case where the response w and the predictors z_i are jointly multivariate normal, the partial regression coefficients are given by equation (27.19) in Kendall and Stuart as a function of second moments of the distribution. In the case where they are not jointly multivariate normal (27.19) is taken to be the definition of partial regression coefficients in the last sentence of Section 27.8 in Kendall and Stuart. Now returning to Section 27.15 in Kendall and Stuart, their equation (27.44) gives the definition of the OLS regression coefficients, also as a function of second moments of the joint distribution of response and predictors, their equation (27.44). This agreement between OLS estimates and partial regression coefficients is the second argument of Kendall and Stuart.

But this second argument also misses the point. The arbitrary definition of partial regression coefficients in the case where the response and predictors are not jointly multivariate normal decouples them from any relationship with conditional expectation. Thus OLS does indeed estimate “partial regression coefficients” but, when the regression function

fails to be linear, so (9) does not hold, these estimates β have nothing to do with the regression function. Returning to fitness landscapes, when the actual fitness landscape $g(z)$ is not linear and so not equal to its best linear approximation $g_1(z)$, then the slope β_1 of the approximation need have no connection with the actual fitness landscape. One would think this is obvious. If β_1 tells us everything we need to know about the actual fitness landscape, why even consider the best quadratic approximation? Perhaps because this argument is wrongheaded?

The current edition of Kendall and Stuart (Stuart et al., 1999) seems to agree with us. Sections 28.12 and 28.13 in the sixth edition correspond to Section 27.15 in the third edition cited by Lande and Arnold. Section 28.13 says

Although there is a difference in interpretation between the linear regressions in [Section] 28.9 and 28.12, we see that the functional form of β is the same and that the LS estimators derived from (28.32) or (28.34) are the same as the ML estimators we obtain from the multinormal case. It follows that the results of this chapter apply whenever the least squares argument can be invoked. In particular, the approximate linear regression derived in [Section] 28.12 is often considered to be *the* regression function, without further qualification; this may be a questionable assumption.

The equivalence is also used to justify the use of partial correlations, whatever the underlying distribution. However, it should be noted that whereas zero partial correlations imply conditional independence for the multinormal, this is *not* true in general.

We take “may be a questionable assumption” and “however, it should be noted” to be academic weasel wording for wrong or at least wrongheaded.

We consider this Section 27.15 of Kendall and Stuart (1973), the one cited by Lande and Arnold (1983), to be the tail end of a century of excuses for using the normal distribution in situations where it was inappropriate. It is hard to imagine a statistician trained after 1973 saying something like what Kendall and Stuart (1973) say. Since 1973 we have had the nonparametrics revolution, which deals with arbitrary regression functions, and the robustness revolution, which deals with non-normal response, and the categorical and GLM revolutions, which deal with discrete response, and the bootstrap revolution, which deals with arbitrary data. No statistician trained in all of these wants an excuse for not using any of them and sticking with what was available in 1973.

In this technical report we are particularly focused on using aster models to improve estimation of fitness landscapes, but even if one were to reject our approach, there are many other areas of modern statistics that can potentially contribute to this area. There is no reason to limit oneself to methods available in 1973.

2 Lande-Arnold Theory

2.1 Best Quadratic Approximation

The best quadratic approximation to the fitness landscape is given by (3b) when α_2 , β_2 , and γ_2 are as defined in the accompanying text. The reason why this approximation is given this name is explained in Section 2.1.3 below.

2.1.1 Existence and Uniqueness of Solutions

By linearity and monotonicity of expectation, the function $Q(\alpha, \beta, \gamma)$ defined by (2) is a convex quadratic function of its arguments assuming second moments of w and fourth moments of z exist. This means solutions α_2 , β_2 , and γ_2 exist. Solutions will be unique if the linear equations that determine a solution, obtained by setting (10a), (10b), and (10c) equal to zero, have unique solutions.

2.1.2 Solutions

To find the solutions we need

$$\frac{\partial Q(\alpha, \beta, \gamma)}{\partial \alpha} = -2E\{w - \alpha - z^T \beta - \frac{1}{2} z^T \gamma z\} \quad (10a)$$

$$\frac{\partial Q(\alpha, \beta, \gamma)}{\partial \beta_i} = -2E\{(w - \alpha - z^T \beta - \frac{1}{2} z^T \gamma z) z_i\} \quad (10b)$$

$$\frac{\partial Q(\alpha, \beta, \gamma)}{\partial \gamma_{jk}} = -E\{(w - \alpha - z^T \beta - \frac{1}{2} z^T \gamma z) z_j z_k\} \quad (10c)$$

Predictors Centered Lande and Arnold (1983) assume that z is multivariate normal with mean vector zero and non-singular variance matrix Σ . Note that (10b) involves third moments of z and (10c) involves fourth moments. By symmetry the odd moments are zero. The second moments are components of the matrix Σ . The fourth moments are given by equation (26) in Anderson (2003)

$$E(z_i z_j z_k z_l) = \sigma_{ij} \sigma_{kl} + \sigma_{ik} \sigma_{jl} + \sigma_{il} \sigma_{jk} \quad (11)$$

where the little sigmas are the components of Σ .

Say $E(w) = \eta$. Setting (10a) equal to zero gives

$$\eta - \alpha - \frac{1}{2} \text{tr}(\gamma \Sigma) = 0$$

(the term involving only first moments of z drops out) and solving for α gives

$$\alpha = \eta - \frac{1}{2} \text{tr}(\gamma \Sigma) \quad (12)$$

Setting (10b) equal to zero gives

$$E\{(w - z^T \beta) z_i\} = 0$$

(the terms involving only first and third moments of z drop out). Rewriting this in vector form gives

$$\text{cov}(w, z) = E(z z^T \beta) = \Sigma \beta$$

and solving for β gives

$$\beta = \Sigma^{-1} \text{cov}(w, z) \quad (13)$$

Setting (10c) equal to zero gives

$$E\{(w - \alpha - \frac{1}{2} z^T \gamma z) z_j z_k\} = 0$$

(the terms involving only third moments of z drop out). Plugging in (12) gives

$$E\left\{(w - \eta + \frac{1}{2} \text{tr}(\gamma, \Sigma) - \frac{1}{2} z^T \gamma z) z_j z_k\right\} = 0 \quad (14)$$

By (11)

$$\begin{aligned} E\{(z^T \gamma z) z_j z_k\} &= \sum_{il} \gamma_{il} E(z_i z_j z_k z_l) \\ &= \sum_{il} \gamma_{il} [\sigma_{ij} \sigma_{kl} + \sigma_{ik} \sigma_{jl} + \sigma_{il} \sigma_{jk}] \\ &= 2(\Sigma \gamma \Sigma)_{jk} + \text{tr}(\gamma \Sigma) \sigma_{jk} \end{aligned}$$

where the first term on the last line means the j, k term of the matrix $\Sigma \gamma \Sigma$. Plugging this back into (14) gives

$$E\{(w - \eta) z_j z_k\} - (\Sigma \gamma \Sigma)_{jk} = 0$$

Rewriting this in vector form gives

$$\text{cov}(w, z z^T) = \Sigma \gamma \Sigma$$

and solving for γ gives

$$\gamma = \Sigma^{-1} \text{cov}(w, z z^T) \Sigma^{-1} \quad (15)$$

Equations (13) and (15) appear in Lande and Arnold (1983).

Equations (13) and (15) are the completion of proofs that $\beta_2 = \beta_4$ and $\gamma_2 = \gamma_4$ in the notation of Section 1.2. Note that the assumptions required for this are that z be multivariate normal with mean vector zero and non-singular variance matrix.

Predictors Not Centered Now we investigate what would happen if we did not assume $E(z) = 0$ but did still assume z was multivariate normal with non-singular variance matrix Σ . Say $E(z) = \mu$. Then $y = z - \mu$ is as z was before. The best quadratic approximation to

$$h(y) = E(w | y)$$

is

$$h_{\text{quad}}(y) = \alpha' + y^T \beta' + \frac{1}{2} y^T \gamma' y$$

where α' is given by (12) and β' and γ' are given by (13) and (15) with z replaced by y . By translation equivariance

$$\begin{aligned} g_{\text{quad}}(z) &= h_{\text{quad}}(z - \mu) \\ &= \alpha' + (z - \mu)^T \beta' + \frac{1}{2} (z - \mu)^T \gamma' (z - \mu) \\ &= \alpha' - \mu^T \beta' + \frac{1}{2} \mu^T \gamma' \mu + z^T \beta' - z^T \gamma' \mu + \frac{1}{2} z^T \gamma' z \end{aligned}$$

from which we see that

$$\alpha_2 = \alpha' - \mu^T \beta' + \frac{1}{2} \mu^T \gamma' \mu \quad (16a)$$

$$\beta_2 = \beta' - \gamma' \mu \quad (16b)$$

$$\gamma_2 = \gamma' \quad (16c)$$

So the values of α and β change depending on whether or not z is centered at zero, but the value of γ does not change. If we think geometrically, the relation $g_{\text{quad}}(z) = h_{\text{quad}}(z - \mu)$ says the two quadratic approximations are essentially the same when we take the shift of the domain into account.

2.1.3 Another Formulation

In this section we consider why the minimizer of the function $Q(\alpha, \beta, \gamma)$ defined by (2) is called the best quadratic approximation to the fitness landscape $g(z)$. That name should be given to (3b) when α_2 , β_2 , and γ_2 are as defined to be the minimizers of

$$\tilde{Q}(\alpha, \beta, \gamma) = E\{(g(z) - \alpha - z^T \beta - \frac{1}{2} z^T \gamma z)^2\} \quad (17)$$

so that $E\{(g(z) - g_2(z))^2\}$ is as small as possible. However, there is no difference between these two definitions of the best quadratic approximation because

$$\begin{aligned} Q(\alpha, \beta, \gamma) &= E\{(w - \alpha - z^T \beta - \frac{1}{2} z^T \gamma z)^2\} \\ &= E\{(w - g(z) + g(z) - \alpha - z^T \beta - \frac{1}{2} z^T \gamma z)^2\} \\ &= E\{(w - g(z))^2\} + 2E\{(w - g(z))(g(z) - \alpha - z^T \beta - \frac{1}{2} z^T \gamma z)\} \\ &\quad + E\{(g(z) - \alpha - z^T \beta - \frac{1}{2} z^T \gamma z)^2\} \\ &= E\{(w - g(z))^2\} + \tilde{Q}(\alpha, \beta, \gamma) \end{aligned}$$

because

$$\begin{aligned} &E\{(w - g(z))(g(z) - \alpha - z^T \beta - \frac{1}{2} z^T \gamma z)\} \\ &= E[E\{(w - g(z))(g(z) - \alpha - z^T \beta - \frac{1}{2} z^T \gamma z) \mid z\}] \\ &= E[(g(z) - \alpha - z^T \beta - \frac{1}{2} z^T \gamma z)E\{w - g(z) \mid z\}] \end{aligned}$$

is zero because $E\{w - g(z) \mid z\} = 0$. Thus $Q(\alpha, \beta, \gamma)$ and $\tilde{Q}(\alpha, \beta, \gamma)$ are minimized at exactly the same values.

2.2 Best Linear Approximation

The best linear approximation is given by (3a) when α_1 and β_1 are as defined in the accompanying text. The reason why this approximation is given this name is explained in Section 2.1.3 above.

2.2.1 Existence and Uniqueness of Solutions

By linearity and monotonicity of expectation, the function $Q(\alpha, \beta, 0)$ obtained by constraining $\gamma = 0$ in (2) is a convex quadratic function of its arguments assuming second moments of w and z exist. This means solutions α_1 and β_1 exist. Solutions will be unique if the linear equations that determine a solution, obtained by setting (18a) and (18b) equal to zero, have unique solutions.

2.2.2 Solutions

To find the solutions we need

$$\frac{\partial Q(\alpha, \beta, 0)}{\partial \alpha} = -2E\{w - \alpha - z^T \beta\} \quad (18a)$$

$$\frac{\partial Q(\alpha, \beta, 0)}{\partial \beta_i} = -2E\{(w - \alpha - z^T \beta)z_i\} \quad (18b)$$

In this section we make no assumptions about the distribution of z (other than existence and non-singularity of certain moments). Setting (18a) equal to zero gives

$$\eta - \alpha - \mu^T \beta = 0$$

where $\mu = E(z)$, and solving for α gives

$$\alpha = \eta - \mu^T \beta \tag{19}$$

Setting (18b) equal to zero gives

$$E\{(w - \alpha - z^T \beta)z_i\} = 0$$

Rewriting this in vector form gives

$$E(wz) - \alpha\mu - E(zz^T)\beta = 0$$

Plugging in (19) gives

$$E(wz) - \eta\mu - [E(zz^T) - \mu\mu^T]\beta = \text{cov}(w, z) - \Sigma\beta = 0$$

and solving for β gives (13).

This completes the proof that $\beta_1 = \beta_4$ in the notation of Section 1.2. Note that no assumptions about the distribution of z were used except for the existence of second moments and non-singularity of Σ .

2.3 Selection Gradients

Now we look at another part of the argument of Lande and Arnold (1983). Define β_3 and γ_3 by (4a) and (4b). By integration by parts, an argument called Stein's lemma (Stein, 1981) by statisticians, we have

$$\begin{aligned} \beta_3 &= - \int g(z) \nabla f(z) dz \\ &= \Sigma^{-1} \int zg(z) f(z) dz \\ &= \Sigma^{-1} \text{cov}\{g(z), z\} \end{aligned}$$

which agrees with (13) by use of the iterated expectation theorem. Throughout this section we assume z is multivariate normal with non-singular variance matrix Σ but make no other assumptions about the marginal distribution of z . We do need some weak assumptions about the conditional distribution of w given z . The assumption used by Lande and Arnold (1983), that $g(z)$ is a bounded function, is overly strong; see Stein (1981) for minimal conditions. Also

$$\begin{aligned} \gamma_3 &= \int g(z) \nabla^2 f(z) dz \\ &= \int [\Sigma^{-1} zz^T \Sigma^{-1} - \Sigma^{-1}] g(z) f(z) dz \\ &= \Sigma^{-1} \text{cov}\{g(z), zz^T\} \Sigma^{-1} \end{aligned}$$

which agrees with (15) by use of the iterated expectation theorem.

This completes the proof that $\beta_3 = \beta_4$ and $\gamma_3 = \gamma_4$ in the notation of Section 1.2. Note that the assumptions required for this are that z be multivariate normal with non-singular variance matrix.

Also note that this argument does not need the assumption $E(z) = 0$. It is clear from geometric considerations that β_3 and γ_3 defined by (4a) and (4b) would not change if the domain (the space where z takes values) is shifted by μ . The relation $g(z) = h(z - \mu)$ implies $\nabla g(z) = \nabla h(z - \mu)$ and $\nabla^2 g(z) = \nabla^2 h(z - \mu)$. Hence $E\{\nabla g(z)\} = E\{\nabla h(y)\}$ and $E\{\nabla^2 g(z)\} = E\{\nabla^2 h(y)\}$, where $y = z - \mu$.

Hence in this section shifting the mean does not change the values of β_3 and γ_3 , but in Section 2.1.2 shifting the mean does change the value of β_2 . Thus we have $\beta_2 = \beta_3$ only when $E(z) = 0$, which, presumably, is one reason why Lande and Arnold (1983) made this assumption, the other reason being to make $\beta_1 = \beta_2$.

2.4 Selection Differentials

In this section we assume $E(w) = 1$ instead of $E(w) = \eta$ we had before. This assumption is announced by calling w *relative fitness*. The remainder of this chapter only concerns β_4 and γ_4 defined by (5a) and (5b) and their relationship to selection.

2.4.1 Directional Selection

Phenotypic The difference between the average value of z before selection and “after selection but before reproduction” (Lynch and Walsh, 1998, p. 46) is

$$E(wz) - E(z) = \text{cov}(w, z). \quad (20)$$

Note that this quantity appears in (13). Lynch and Walsh (1998) call (20) the *Robertson-Price identity*, and Lande and Arnold (1983) call it “a multivariate generalization of the results of Robertson (1966) [cited in Price (1972)] and Price (1970, 1972).” It is not clear what the phrase “after selection but before reproduction” can mean in natural populations where selection includes differential reproduction, but the mathematical meaning of the left hand side of (20) is clear: the difference between the weighted average of phenotype values, weighted according to relative fitness, and the unweighted average. That this may be an important quantity for describing selection, we do not dispute, whether or not it corresponds in reality to a difference of average phenotype values at any two specified points in the life cycle.

In fact what Price (1972) calls “type I selection” is more general than what is discussed by Lande and Arnold (1983) and Lynch and Walsh (1998), it being “a far broader problem category than one might at first assume” but “intended mainly for use in deriving general relations and constructing theories, and to clarify understanding of selection phenomena, rather than for numerical calculation” (both quotations from Price, 1972). The reason for the discrepancy between the narrow applicability of the theory in Lande and Arnold (1983) and the broad applicability of Price (1972) is that the theory in Price (1972) is more general: our (20) corresponds to (A 13) in Price (1972) but this is only a limited special case of his (A 11) which contains an extra term on the right-hand side. This extra term, which is hard

to estimate, accounts of the theory of (A 11) being not for numerical calculation, where the limited special case can be so used.

Genetic Now suppose a quantitative genetic model

$$z = x + e$$

where x is the vector of additive genetic effects, e is everything else (environmental, non-additive genetic, and gene-environment interaction effects), and x and e are assumed to be independent with

$$x \sim \text{Normal}(\mu, G)$$

$$e \sim \text{Normal}(0, E)$$

where G is the “G matrix” (additive genetic variance-covariance matrix) and E is another variance-covariance matrix. This makes the regression of breeding values x on phenotypic characters z linear and homoscedastic (Lande and Arnold, 1983, equation (3b)). More precisely, the conditional distribution of x given z is multivariate normal with

$$E(x | z) = \mu + G\Sigma^{-1}(z - \mu) \quad (21a)$$

$$\text{var}(x | z) = G - G\Sigma^{-1}G \quad (21b)$$

(Anderson, 2003, equations (5) and (6) of Section 2.5).

We also need to assume that x and w are conditionally independent given z , which is a very strong assumption. An equivalent way to state this is that the conditional distribution of w given x and z does not actually depend on x , that is, genotypic characters x influence fitness only through the values of the phenotypic characters z .

Then the difference of genotypic values before selection and after selection but before reproduction is

$$\begin{aligned} E(wx) - E(x) &= E\{E(wx | z)\} - \mu \\ &= E\{E(w | z)E(x | z)\} - \mu \\ &= E\{E(w | z)[\mu + G\Sigma^{-1}(z - \mu)]\} - \mu \\ &= E\{E(w[\mu + G\Sigma^{-1}(z - \mu)] | z)\} - \mu \\ &= E\{w[\mu + G\Sigma^{-1}(z - \mu)]\} - \mu \\ &= G\Sigma^{-1} \text{cov}(w, z) \end{aligned} \quad (22)$$

which is equation (6a) in Lande and Arnold (1983). The conditional independence of x and w given z is the second equality in (22). Note that the right-hand side here is again related to (13).

2.4.2 Stabilizing and Disruptive Selection

Phenotypic If we play the same game with variance instead of means, the variance “after selection, but before reproduction” is

$$E\{w(z - \zeta)(z - \zeta)^T\}$$

where $\zeta = E(wz)$ is the mean “after selection but before reproduction”. To follow Lande and Arnold (1983) we need a notation for (20). They use $s = \text{cov}(w, z)$ and we will follow them. Thus we are using Greek letters for all parameters except for E , G and s . Then $\zeta = \mu + s$, and

$$\begin{aligned} E\{w(z - \zeta)(z - \zeta)^T\} &= E\{w(z - \mu - s)(z - \mu - s)^T\} \\ &= E\{w(z - \mu)(z - \mu)^T\} - 2E\{w(z - \mu)\}s^T + ss^T \\ &= E\{w(z - \mu)(z - \mu)^T\} - ss^T \end{aligned}$$

and the stabilizing or disruptive selection differential is

$$\begin{aligned} E\{w(z - \zeta)(z - \zeta)^T\} - \text{var}(z) &= E\{w(z - \mu)(z - \mu)^T\} - ss^T - \Sigma \\ &= \text{cov}\{w, (z - \mu)(z - \mu)^T\} - ss^T \end{aligned} \quad (23)$$

which is equation (13a) in Lande and Arnold (1983). In the case $\mu = 0$, note that (23) contains $\text{cov}(w, zz^T)$ which also appears in (15), which was derived under the assumption $\mu = 0$.

Genetic If we play the same game with genotypes x rather than phenotypes z , the quantity we want to obtain is

$$E\{w(x - \xi)(x - \xi)^T\} - \text{var}(x) \quad (24)$$

where

$$\xi = E(wx) = \mu + G\Sigma^{-1} \text{cov}(w, z) = \mu + G\Sigma^{-1}s. \quad (25)$$

Now

$$\begin{aligned} E\{w(x - \xi)(x - \xi)^T\} &= E\{w(x - \xi)(x - \xi)^T \mid z\} \\ &= E\{E(w \mid z)E[(x - \xi)(x - \xi)^T \mid z]\} \\ &= E\{wE[(x - \xi)(x - \xi)^T \mid z]\} \end{aligned} \quad (26)$$

The conditional independence of x and w given z is the second equality in (26). And

$$E[(x - \xi)(x - \xi)^T \mid z] = \text{var}(x \mid z) + E(x - \xi \mid z)E(x - \xi \mid z)^T$$

where $\text{var}(x \mid z)$ is given by (21b) and from (21a) and (25) we have

$$\begin{aligned} E(x - \xi \mid z) &= \mu + G\Sigma^{-1}(z - \mu) - \xi \\ &= \mu + G\Sigma^{-1}(z - \mu) - (\mu + G\Sigma^{-1}s) \\ &= G\Sigma^{-1}(z - \mu - s) \\ &= G\Sigma^{-1}(z - \zeta) \end{aligned}$$

Hence

$$E[(x - \xi)(x - \xi)^T \mid z] = G - G\Sigma^{-1}G + G\Sigma^{-1}(z - \zeta)(z - \zeta)^T\Sigma^{-1}G$$

and (24) becomes

$$\begin{aligned}
E\{w(x - \xi)(x - \xi)^T\} - \text{var}(x) &= E\{wE[(x - \xi)(x - \xi)^T | z]\} - G \\
&= E\{w[G - G\Sigma^{-1}G + G\Sigma^{-1}(z - \zeta)(z - \zeta)^T\Sigma^{-1}G]\} - G \\
&= -G\Sigma^{-1}G + G\Sigma^{-1}E\{w(z - \zeta)(z - \zeta)^T\}\Sigma^{-1}G \\
&= -G\Sigma^{-1}G + G\Sigma^{-1}[\text{cov}\{w, (z - \mu)(z - \mu)^T\} - ss^T + \Sigma]\Sigma^{-1}G \\
&= G\Sigma^{-1}[\text{cov}\{w, (z - \mu)(z - \mu)^T\} - ss^T]\Sigma^{-1}G
\end{aligned} \tag{27}$$

where the next to last equality plugs in (23). This agrees with equation (12) of Lande and Arnold (1983).

2.4.3 Discussion of Selection Differentials

The phenotypic directional selection differential (20) is part of the formula for β_4 given by (5a). Conversely, the formula for β_4 is part of the formula for the genetic directional selection differential given by (22).

The phenotypic stabilizing or disruptive selection differential (23) has some relationship to the formula for γ_4 given by (5b), although the relationship is rather vague: the covariance term in (23) is equal to the covariance term in (5b) in the case $E(z) = 0$, but the other parts of these expressions differ. Conversely, the formula for γ_4 is part of the formula for the genetic stabilizing or disruptive selection differential given by (27) in the case $E(z) = 0$.

As seen from our use of "part of the formula" in three cases and even vaguer relationship in the fourth case, the connection between β_4 and γ_4 and these selection differentials is rather vague. Moreover, Lande and Arnold (1983) argue that the betas and gammas are more direct indicators of selection than these selection differentials. Consider the phenotypic directional selection differential $\text{cov}(w, z)$. A component of z that is not under direct selection will nevertheless be correlated with w if it is correlated with other components of z that are under direct selection. Conversely, if a component of z , say z_k , is not under direct selection, then the fitness landscape $g(z)$ is not a function of z_k and $\partial g(z)/\partial z_k = 0$ and the k -th component of β_3 given by (4a) will be zero.

From our point of view, this last argument tells us we should focus on the fitness landscape itself. The various betas and gammas do not provide as much information as good estimates of the fitness landscape. Nor do the selection differentials discussed in this section.

3 Lande-Arnold Analysis versus Fitness Landscapes

3.1 Multivariate

Suppose z is multivariate normal with mean vector μ_1 and variance matrix (variance-covariance matrix, dispersion matrix) Σ_1 . The density of z is

$$f(z) = c_1 \exp \left\{ -\frac{1}{2}(z - \mu_1)' \Sigma_1^{-1} (z - \mu_1) \right\} \tag{28}$$

where c_1 is a constant. Suppose, for reasons of mathematical convenience (to obtain an example we can analyze) the relative fitness landscape has the same form

$$g(z) = c_2 \exp \left\{ -\frac{1}{2}(z - \mu_2)' \Sigma_2^{-1} (z - \mu_2) \right\} \quad (29)$$

where c_2 is another constant, Σ_2 is a symmetric matrix, not necessarily positive definite (more on this below), and μ_2 is an arbitrary vector. Then

$$f(z)g(z) = c_3 \exp \left\{ -\frac{1}{2}(z - \mu_3)' \Sigma_3^{-1} (z - \mu_3) \right\} \quad (30)$$

where

$$\Sigma_3^{-1} = \Sigma_1^{-1} + \Sigma_2^{-1} \quad (31a)$$

$$\mu_3 = \Sigma_3(\Sigma_1^{-1}\mu_1 + \Sigma_2^{-1}\mu_2) \quad (31b)$$

and c_3 is another constant. In order that $g(z)$ be the relative fitness landscape, $f(z)g(z)$ must integrate to one, so c_3 is the normalizing constant of the multivariate normal density with mean vector μ_3 and variance matrix Σ_3 . Also Σ_3 must be positive definite. This places a complicated requirement on Σ_2 via (31a). Although, Σ_2 need not be positive definite, it must combine with Σ_1 to produce a positive definite Σ_3 .

Now let us assume $\mu_1 = 0$ so that from the theory in the preceding chapter we have $\beta_1 = \beta_2 = \beta_3 = \beta_4$ and $\gamma_2 = \gamma_3 = \gamma_4$ so we need not distinguish which betas and gammas we mean and shall just write β and γ with no subscripts for the rest of this chapter.

Differentiating (29) we get

$$\nabla g(z) = -g(z) \Sigma_2^{-1} (z - \mu_2) \quad (32a)$$

$$\nabla^2 g(z) = g(z) \Sigma_2^{-1} (z - \mu_2)(z - \mu_2)' \Sigma_2^{-1} - g(z) \Sigma_2^{-1} \quad (32b)$$

Then using the formulas (4a) and (4b) and the fact that (30) is a normal probability density we can now calculate

$$\beta = -\Sigma_2^{-1}(\mu_3 - \mu_2) \quad (33a)$$

$$\gamma = \Sigma_2^{-1} \Sigma_3 \Sigma_2^{-1} + \Sigma_2^{-1}(\mu_2 - \mu_3)(\mu_2 - \mu_3)' \Sigma_2^{-1} - \Sigma_2^{-1} \quad (33b)$$

It should be clear from the complexity of these formulas that the relationship between the function $g(z)$ and β and γ is anything but simple.

Whether the fitness landscape $g(z)$ has a maximum, a minimum, or a saddle point at μ_2 depends on the signature (the numbers of positive, negative, and zero eigenvalues) of the matrix Σ_2 . If the matrix γ is to provide the same information, it must have the same signature, and this need not happen.

3.2 Univariate

Let us simplify to the case where z is univariate. We keep the assumption $\mu_1 = 0$. Also we replace Σ_i by v_i . Here v is for "variance" but recall that v_2 is not required to be positive, although v_1 and v_3 are required to be positive. Then (33a) and (33b) become

$$\beta = -\frac{\mu_3 - \mu_2}{v_2} \quad (34a)$$

$$\gamma = \frac{v_3 - v_2 + (\mu_2 - \mu_3)^2}{v_2^2} = \frac{v_3 - v_2}{v_2^2} + \beta^2 \quad (34b)$$

and (31a) and (31b) become

$$\frac{1}{v_3} = \frac{1}{v_1} + \frac{1}{v_2} \quad (35a)$$

$$\mu_3 = \frac{v_3 \mu_2}{v_2} \quad (35b)$$

(recall $\mu_1 = 0$). Plugging (35a) and (35b) into (34a) and (34b) gives

$$\beta = \frac{\mu_2}{v_1 + v_2} \quad (36a)$$

$$\gamma = -\frac{1}{v_1 + v_2} + \beta^2 \quad (36b)$$

Clearly, in this simple case β has the “right sign” (same as μ_2), but γ need not have the right sign (same as v_2).

This is just a particular, easy to analyze, special case. In general, if one does not know the functional form of the fitness landscape $g(z)$, one has no knowledge of the relationship between $g(z)$ and β and γ even when we assume that z is multivariate normal with mean zero so all of the betas are equal and all of the gammas are equal. In even more generality, when one does not know the distribution of z , one has no knowledge of the relationship between $g(z)$ and any of the four betas and three gammas, none of which are equal except $\beta_1 = \beta_4$.

3.3 Normalizing Constants

We were a bit cavalier in the preceding two sections about the constants c_1 , c_2 , and c_3 . They are not needed to calculate α , β , and γ and the best quadratic approximation. However, if we want to compare the best quadratic approximation with the actual fitness landscape $g(z)$, then we need to know c_2 . So we calculate that here.

First, from the definition of the normal density

$$c_1 = (2\pi)^{-d/2} \det(\Sigma_1)^{-1/2}$$

$$c_3 = (2\pi)^{-d/2} \det(\Sigma_3)^{-1/2}$$

where d is the dimension of z and \det indicates the determinant.

Hence, combining (28), (29), and (30), we obtain

$$c_3 \exp \left\{ -\frac{1}{2} (z - \mu_3)' \Sigma_3^{-1} (z - \mu_3) \right\}$$

$$= c_1 c_2 \exp \left\{ -\frac{1}{2} (z - \mu_1)' \Sigma_1^{-1} (z - \mu_1) - \frac{1}{2} (z - \mu_2)' \Sigma_2^{-1} (z - \mu_2) \right\}$$

This must hold for all z , hence for $z = 0$, that is,

$$c_3 \exp \left\{ -\frac{1}{2} \mu_3' \Sigma_3^{-1} \mu_3 \right\} = c_1 c_2 \exp \left\{ -\frac{1}{2} \mu_1' \Sigma_1^{-1} \mu_1 - \frac{1}{2} \mu_2' \Sigma_2^{-1} \mu_2 \right\}$$

Hence

$$c_2 = \frac{c_3}{c_1} \exp \left\{ -\frac{1}{2} \mu_3' \Sigma_3^{-1} \mu_3 + \frac{1}{2} \mu_1' \Sigma_1^{-1} \mu_1 + \frac{1}{2} \mu_2' \Sigma_2^{-1} \mu_2 \right\}$$

which simplifies in the univariate case with $\mu_1 = 0$ to

$$c_2 = \sqrt{\frac{v_1}{v_3}} \exp \{ -\mu_3^2/2v_3 + \mu_2^2/2v_2 \}$$

which, plugging in (35b), further simplifies to

$$c_2 = \sqrt{\frac{v_1}{v_3}} \exp \{ \mu_2^2(v_2 - v_3)/2v_2^2 \} \quad (37)$$

3.4 Examples

We give a few examples of the theory in the preceding sections. First example

```
> v1 <- 1
> mu2 <- 0
> v2 <- 2
> beta <- mu2/(v1 + v2)
> gamma <- beta^2 - 1/(v1 + v2)
> alpha <- 1 - gamma * v1/2
> v3 <- 1/(1/v1 + 1/v2)
> c2 <- sqrt(v1/v3) * exp(mu2^2 * (v2 - v3)/(2 * v2^2))
```

Figure 1 (page 18) is made by the following code

```
> zlim <- 3
> foo <- function(z) alpha + beta * z + gamma * z^2/2
> bar <- function(z) c2 * exp(-(z - mu2)^2/(2 * v2))
> zzzz <- seq(-zlim, zlim, 0.01)
> ylim <- c(min(foo(zzzz), bar(zzzz)), max(foo(zzzz),
+ bar(zzzz)))
> curve(foo, col = "magenta", ylab = "relative fitness",
+ xlab = "z", from = -3, to = 3, ylim = ylim, lwd = 2)
> curve(bar, col = "green3", add = TRUE, lwd = 2)
```

Second example

```
> v1 <- 1
> mu2 <- 1
> v2 <- 2
> beta <- mu2/(v1 + v2)
> gamma <- beta^2 - 1/(v1 + v2)
> alpha <- 1 - gamma * v1/2
> v3 <- 1/(1/v1 + 1/v2)
> c2 <- sqrt(v1/v3) * exp(mu2^2 * (v2 - v3)/(2 * v2^2))
```

Figure 2 (page 19) is made by the following code

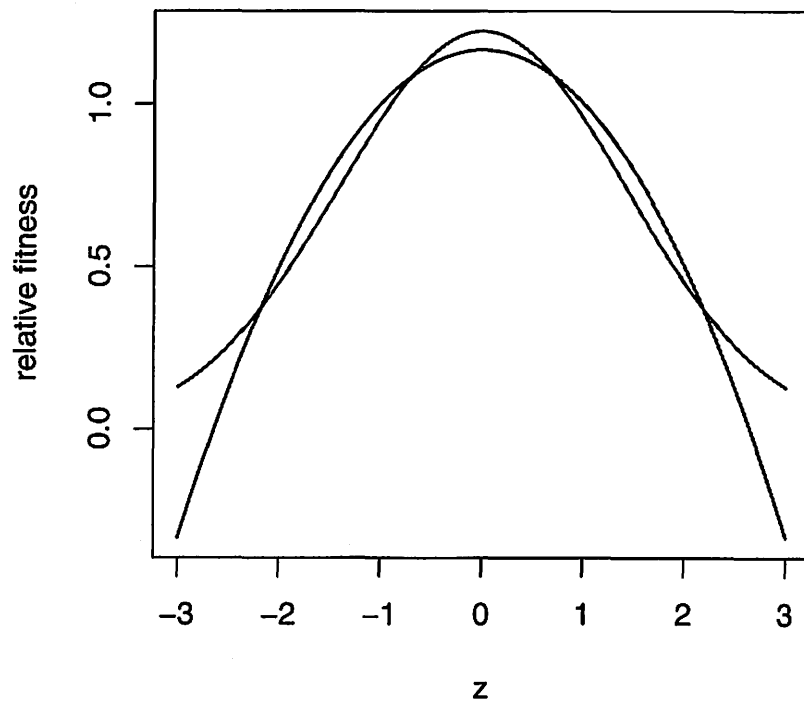


Figure 1: Fitness landscape (green) and its best quadratic approximation (magenta).

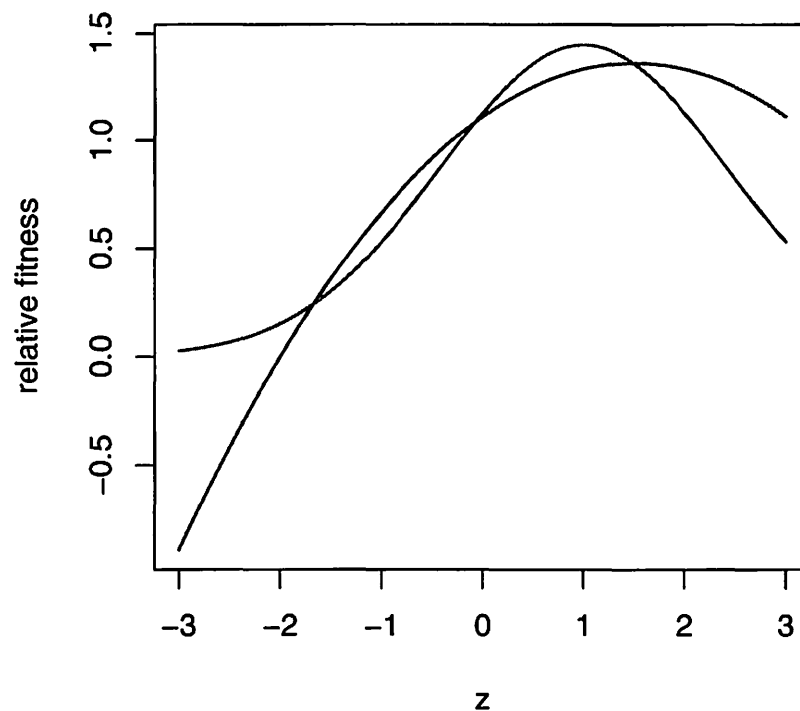


Figure 2: Fitness landscape (green) and its best quadratic approximation (magenta).

```
> foo <- function(z) alpha + beta * z + gamma * z^2/2
> bar <- function(z) c2 * exp(-(z - mu2)^2/(2 * v2))
> ylim <- c(min(foo(zzzz), bar(zzzz)), max(foo(zzzz),
+      bar(zzzz)))
> curve(foo, col = "magenta", ylab = "relative fitness",
+      xlab = "z", from = -3, to = 3, ylim = ylim, lwd = 2)
> curve(bar, col = "green3", add = TRUE, lwd = 2)
```

Third example

```
> v1 <- 1
> mu2 <- 2
> v2 <- 2
> beta <- mu2/(v1 + v2)
> gamma <- beta^2 - 1/(v1 + v2)
> alpha <- 1 - gamma * v1/2
```

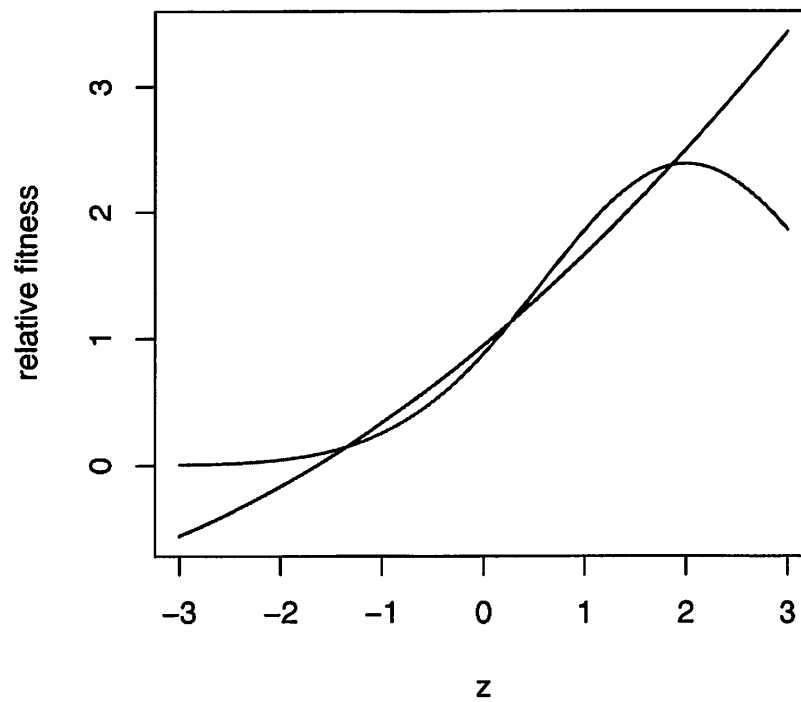


Figure 3: Fitness landscape (green) and its best quadratic approximation (magenta).

```
> v3 <- 1/(1/v1 + 1/v2)
> c2 <- sqrt(v1/v3) * exp(mu2^2 * (v2 - v3)/(2 * v2^2))
```

Figure 3 (page 20) is made by the following code

```
> foo <- function(z) alpha + beta * z + gamma * z^2/2
> bar <- function(z) c2 * exp(-(z - mu2)^2/(2 * v2))
> ylim <- c(min(foo(zzzz), bar(zzzz)), max(foo(zzzz),
+      bar(zzzz)))
> curve(foo, col = "magenta", ylab = "relative fitness",
+      xlab = "z", from = -3, to = 3, ylim = ylim, lwd = 2)
> curve(bar, col = "green3", add = TRUE, lwd = 2)
```

4 Discussion

The main goal of the authors is, admittedly, to foster their own approach to estimation of fitness landscapes (Shaw, et al., 2008), but the main goal of this particular document is to delve deeply into the theory of Lande-Arnold analysis to see what it does and what it cannot possibly do, not without being changed into something completely different.

We, of course, emphasize quite different points from those emphasized by Lande and Arnold (1983). We stress the following. Lande and Arnold (1983) introduce β the *directional selection gradient* and γ the *stabilizing or disruptive selection gradient*, but we point out that they really define four betas and three gammas, and they are quite distinct except when the phenotypic covariates are exactly multivariate normal. Since there is no existing methodology for transforming data to exact multivariate normality, these betas and gammas are best thought of as distinct parameters. Partly because it directly competes with aster analysis, we find the notion of best quadratic approximation Phillips and Arnold (1989), which involves β_2 and γ_2 , the interpretation of Lande-Arnold analysis that is most interesting. This does also seem to be the interpretation of interest to most of the huge literature citing Lande and Arnold (1983).

As we show in Section 3, if one looks carefully at how best quadratic approximation (BQA) actually approximates functions that are possible fitness landscapes, one sees that, although BQA is not uniformly bad, it can be very bad approximation in some circumstances. Since the Lande-Arnold method estimates the BQA of the fitness landscape rather than the fitness landscape itself and since the BQA can be a badly biased approximation of the fitness landscape, one can never know from looking at the BQA alone (much less its OLS estimate) what features of the BQA are reflective of the actual fitness landscape and what features of the BQA are approximation artifacts. Thus one can never know how safe it is to interpret a particular aspect of the BQA as reflecting the underlying biology, since it may be only an artifact of the bias of the BQA.

This is not a mere theoretical quibble. To date only one real data set has been analyzed using both the Lande-Arnold method and the newer aster method (Shaw, et al., 2008), and in this example Lande-Arnold analysis indicates disruptive selection for one phenotypic character whereas aster analysis indicates stabilizing selection for that character. This is exactly what is illustrated in Figure 3 where the true fitness landscape (green curve) has a maximum near the right side of the figure and the BQA (magenta curve) has a minimum somewhere off the left side of the plot. In the terminology of Lande and Arnold, the BQA indicates disruptive selection whereas the actual fitness landscape exhibits only stabilizing selection: by construction, the fitness landscape has a single local maximum, which is also the global maximum, at $z = 2$, what else can one call this? Of course, the selection is mainly directional, but between stabilizing and disruptive, stabilizing is the correct choice.

Section 3 gives a large family of examples, multivariate as well as univariate, that one can play with to see exactly what biases BQA induces in various situations. So long as no one had looked at the biases of BQA in detail, it was possible to maintain the illusion that BQA usually was good enough approximation. Now that the issue has been raised and thoroughly explored, the illusion has been destroyed. Now one must consider in each application of the Lande-Arnold method how bad the biases of BQA may be. Furthermore, to the extent that one is interested in the other parameters, that we called β_3 and γ_3 and

β_4 and γ_4 , one must consider how different they may be from β_2 and γ_2 , which are what the Lande-Arnold procedure estimate unbiasedly.

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